



Anti-sense And Common-sense: Regulation of Food From Genetically Engineered Plants

Citation

Anti-sense And Common-sense: Regulation of Food From Genetically Engineered Plants (1994 Third Year Paper)

Permanent link

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:8889464>

Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

Share Your Story

The Harvard community has made this article openly available.
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

Genetic engineering technology has recently generated techniques for making specific and precise alterations to the genetic composition of crops grown as food for humans and animals. These advances should facilitate the development of crops with enhanced resistance to diseases, pests and bad weather, improved tolerance of environmentally safer herbicides, and greater nutritional value. However, the very power of these techniques has raised fears of potential ecological catastrophe, as well as religious and aesthetic questions that arise from the prospect of vegetables containing genes ultimately derived from fish and animals. This essay briefly reviews the nature of the technology and its potential benefits and risks. It then discusses the regulatory framework with particular emphasis on the regulatory strategy adopted by FDA. Finally, it suggests that FDA's stance, while legally and scientifically defensible, is strategically misconceived in that stricter regulation would promote public acceptance of this technology.

Nature of the technology

Mankind has been manipulating food crops for millennia. All modern staple crops are derived from originally wild varieties domesticated by man and propagated far beyond their natural ecological niches. Human intervention was limited at first to artificial selection of variants occurring through natural mutation and gene rearrangement. The discovery of Mendelian genetics in the last century made possible rationally directed breeding programs. Though scientific principles now informed the selection of hybrids and generation of true-breeding strains, traditional breeding still depended on naturally occurring variations; hybrids could be generated only by

ID # 103-8585-7 1

crossing variants of the same species. Nevertheless, traditional breeding techniques have resulted in dramatic changes in foods: for instance, a small berry native to Asia (chinese gooseberry) was transformed into the large kiwifruit now popular in America and Europe.¹

Biotechnology has been applied to food crops in two successive waves. Old biotechnology employs artificial techniques to increase variation in target plants (so as to enhance the likelihood of finding a desirable trait) and to facilitate transfer of genes across the species barrier. Thus, random mutations are induced by treatment with chemicals or irradiation (mutagenesis) or facilitated by cloning cells from cultures of callus or leaf (somaclonal variation). Fertile progeny can be derived from wide crosses (between different species) by techniques such as embryo rescue and chromosomal doubling ●2

New biotechnology uses genetic engineering techniques to select genes encoding desirable traits and introduce them into cells of host plants in which these traits are desired. By culturing whole plants from these altered cells, transgenic plant lines can be produced that contain the inserted gene in every cell and transmit the inserted gene to every successive generation. These genetic engineering techniques represent a powerful advance in two respects. First, it is now possible to select and insert a desirable gene without simultaneously introducing other, undesirable traits that must later be eliminated through traditional breeding (or tolerated). Second, the species barrier is eradicated. Plants can receive genes from viruses, bacteria, other plants or animals (including man).

The inserted genetic material is laboratory-made and consists of the gene encoding the desired trait together with additional genetic material to achieve permanent incorporation into cells of the host plant and efficient expression of the desired trait. Currently, these workhorse genes are derived from bacteria that naturally infect plants – a fact that has regulatory consequences. In

addition, current technology requires insertion of an additional gene to permit selection of those few altered cells that receive functioning inserted genetic material for further study. After this initial selection, the marker gene plays no useful role, but nevertheless continues functioning in every cell of every plant in every subsequent generation. Since the marker currently used is an antibiotic-resistance gene derived from a bacterium that commonly causes disease in humans, this aspect of the technique presents a regulatory issue.

Potential benefits of the technology

Genetic engineering techniques vastly expand the repertoire of alterations that are feasible in food crops. By 1992, over 30 transgenic crops were being field tested.³ The front runner, the Flavr Savr tomato developed by Calgene, illustrates the commercial potential of even elementary modifications. In order to slow down the process of ripening and softening that eventually renders tomatoes unfit for sale, Calgene isolated the gene encoding an enzyme responsible for this process (polygalacturonase, PG) and inserted it backwards (antisense). When the normal gene becomes active during ripening and produces the chemical message (mRNA) that would normally cause the cells to make the PG enzyme, this message complexes with the product of the antisense gene and is rapidly destroyed. Since the cells are unable to make PG, softening is greatly retarded, and spoilage of the vine-ripened tomatoes correspondingly reduced. The firmer texture of these tomatoes is also valued in processing. In several ways, this is an ideal test product. The desired trait depends not on introducing a protein derived from other plants or from animals, but on preventing the appearance of a tomato protein. Calgene has subjected its product to extensive testing, including full characterization of the inserted genetic construct to prove its stability and extensive toxicological analysis on the individual tomato variants developed.

Other proposed applications are even more ambitious and offer tantalizing prospects for

ID # 103-8585-7

3

solving ecological and nutritional problems of both the industrialized and the developing world.⁴ Crops can be made resistant to insect pests, e.g. by introducing genes encoding a selectively toxic bacterial protein (the Bt protein) that does not affect mammals, fish, plants or beneficial insects. Resistance could be conferred against plant viruses and against adverse weather conditions such as frost and changes in temperature. There are proposals to develop salt-tolerant crops that could be grown in arid regions upon irrigation with pure or partly desalinized sea-water. Altered feed crops are being developed with increased amounts of essential amino acids such as lysine and methionine. Similar modifications to staple crops could do much to alleviate protein malnutrition in the developing world. Foods being modified to combat diseases of industrialized nations include strawberries rich in the cancer-protective agent ellagic acid, and rapeseed enriched in unsaturated fats as a source of healthier canola oil. Crops that can fix nitrogen (or that harbor nitrogen-fixing bacteria, as legumes do) would decrease the need for artificial fertilizers, benefiting the ecology of industrialized nations and the food supply of developing ones. Crops that resist broad-spectrum herbicides will permit the use of environmentally friendly herbicides chosen for their rapid disappearance from the soil rather than their narrow killing spectrum.

Contrary to the claims of some critics, the economics of genetic engineering suggest benefits for the developing world. The nature of the technology requires great sophistication to produce transgenic plants but not to exploit them. Crops could be custom-made in western laboratories and the seeds distributed directly to farmers in the developing world, making this a highly sophisticated yet fully appropriate technology. Presumably western donor governments would be disposed to fund aid projects that directly benefitted not merely their domestic economies but also the biotechnology sector they have targeted for promotion.

ID # 103-8585-7

4

Potential risks of the technology

(I) Risks arising from cultivation

Genetic material in transgenic crops is transmitted to successive generations of the transgenic crop itself and has the potential to spread through cross-pollination to native (non-transgenic) variants of the same species (whether cultivated or wild) and to other sexually compatible species.³ Contamination of native seeds with seeds from transgenic variants will produce mixed crops in the next generation; it is likely that native and transgenic seeds and plants will be indistinguishable to the native eye. In this way, transgenic crops could enter the food supply unrecognized, frustrating attempts to track and label them.

Inserted genetic material could also be acquired by bacteria or viruses that infect the transgenic plants (horizontal transfer); these micro-organisms could conceivably act as vectors to convey the genetic constructs to other plants. Though theoretically valid, these events are probably very infrequent; moreover, the same potential exists for genes native to the plant. The one exception to this complacent assessment is the antibiotic resistance gene inserted as a marker for the genetically altered cells. This gene is derived from bacteria, which transfer antibiotic resistance genes amongst one another. Antibiotic resistance would confer a selective advantage on bacteria in settings where use of that antibiotic is widespread. USDA has accepted calculations, based on a worst case scenario, that even if such transfers occur the antibiotic-resistant soil bacteria that result would represent 1.4×10^6 of the resistant microbes already present.⁶

Genetic manipulation of plants may confer a competitive advantage and create the potential for growth as a weed. This is likeliest with alterations that confer resistance to pests or chemicals or reduce the need for fertilizers, and is a major consideration in USDA regulatory policy.

(2) Risks arising from use as food or food components

ID # 103-8585-7

5

Genetic alteration of food crops may introduce toxic substances, reduce the nutritional value of food, introduce proteins capable of provoking allergic responses, or reduce the effectiveness of certain antibiotics.

Many plants contain toxic substances. Most edible plants, when ripe, have low enough levels of poisons to permit safe ingestion; in some (such as cassava and some legumes) proper preparation is required before the food can be safely eaten. Genetic manipulation could introduce toxic substances or increase their concentration by a variety of mechanisms. Interfering with the normal ripening process could prevent the normal decrease in toxic substances that accompanies ripening. For instance, tomatoes belong to the same plant family as the Deadly Nightshade; the Flavr Savr tomato was specifically tested for tomatine and other potentially poisonous glykoalkaloids in ripe and green fruit, for each line to be commercialized.⁷ Introduced substances that are innocuous in the donor plant could be metabolized differently by the host, with toxic results. The introduced genetic material, which by current techniques is inserted at a random site in the host's genes, may by chance inactivate a metabolic pathway required to neutralize a toxic intermediate or may reactivate a toxic pathway silenced during evolution.

By similar mechanisms, genetic manipulation may reduce the nutritional value of food either by altering the level or bioavailability of important nutrients or by altering the chemical nature of important nutrients. If this technology had arisen before we realized the importance of saturated fats in contributing to heart disease and certain cancers, it is unlikely that transgenic plants would have been monitored for alterations in these components; one can only speculate about other aspects of nutrition that we currently fail to monitor through ignorance.

Food allergy is well recognized, but imperfectly understood. It is highly idiosyncratic. The propensity for allergic reactions runs in families, but the provoking allergens differ for each

ID # 103-8585-7 6

individual and are discovered by trial and error. Allergic individuals are counselled to avoid foods known to be allergenic to them. Some foods (e.g. shellfish, nuts) commonly provoke allergic reactions. In some cases the provoking allergen – generally a protein – is known (e.g. gluten in wheat), but in most cases it is not. While tests with allergic volunteers can identify major allergenic components, the idiosyncratic nature of allergy dictates that a food can never be pronounced free of introduced allergens for an particular allergic individual. Allergic consumers always eat any new food at the risk of provoking a reaction; only a warning that the food has been genetically engineered (and disclosing the origin of any protein introduced) can trigger the appropriate precautions.

Potential interference with antibiotics has become a heated topic. Currently technology requires the introduction of an antibiotic resistance gene as a marker for transfected cells. The 30 products closest to market use the *kad* gene (which encodes the enzyme kanamycin phosphotransferase II and confers resistance to medically important antibiotics such as kanamycin and neomycin). Both the *kanr* gene and its enzyme product will be present in food derived from the transgenic plants, raising the possibility that the enzyme may interfere with orally administered kanamycin or neomycin, and that the gene may be transferred to gut bacteria and make them resistant. FDA appears to accept that the enzyme represents little danger, since it will be digested like any other protein and even while intact would not be able to act in the chemical environment of the gut. Moreover, these antibiotics are poorly absorbed and are rarely given orally.’ FDA responded less convincingly to the issue raised by the gene when it pointed to widespread topical use of neomycin-containing ointments as a major factor in inducing resistance. The agency has not explained why these ointments should not be restricted from OTC use rather than used as the predicate for promoting yet more resistance to an important group of antibiotics, commonly used

for intravenous therapy of life-threatening infections.

(3) Religious, aesthetic and ecological concerns

Transferring genes across species raises religious and aesthetic concerns. Consumers who avoid certain species on religious grounds (pigs for Muslims, cows for Hindus, various species of animals, fish and crustaceans for Jews) or for moral or aesthetic reasons (vegetarians, vegans) must confront the issues raised by genetically engineered plants that express genes originally derived from animal species. Most people might feel qualms about eating plants whose genes were partly human. FDA has taken the position that scientists do not infuse the plant with the original genes that were removed from the animal and that there is no scientific evidence that such genetic alterations change the essential nature of the plant or confer animal-like characteristics.⁹ The agency therefore concludes that information on the label disclosing the use of genetic engineering and indicating the transgene's origin would not be material, no matter how earnestly consumers desire it. This is a callous and glib response to issues that are religious and aesthetic rather than scientific and on which FDA manifestly lacks expertise.

Critics have raised concerns about the economic impact of high technology crops that would benefit large agricultural producers over small farmers, and industrialized nations over third world agricultural exporters. Commentators have pointed to secondary ecological effects such as promoting increased use of toxic chemicals¹⁰ and reducing ecological diversity.

Regulatory strategy of USDA

Regulation by USDA is aimed at protecting agriculture from harmful effects of genetically engineered crops, concerns distinct from their regulation as food. However, comparison of the regulatory strategy of USDA and FDA reveals distinctly different approaches by two agencies both eager to promote this technology and reluctant to burden it with unnecessary regulation. Despite

ID # 103-8585-7

8

FDA's primary mandate to promote the safety of the food supply, it is USDA that adopted the more active monitoring role. Paradoxically, it appears that closer regulation along the USDA model may promote rather than retard this new industry.

USDA has asserted jurisdiction over transgenic crops under the Federal Plant Pest Act, 7 U.S.C. §151-164a, 166-167I2. This jurisdiction is based primarily on the presence of inserted genetic material derived originally from bacteria or viruses that infect plants. In general, prior approval (by obtaining a permit) is needed before a genetically engineered plant can be introduced into agriculture, whether for field testing or commercial farming. However, certain host species have been designated as having negligible risk for inadvertent transfer of inserted genes to other crops. Genetically engineered variants of these species (corn, cotton, potato, soybean, tobacco, tomato) can be introduced without prior approval provided USDA is notified in the prescribed form. Moreover, an interested party can petition for deregulation of a particular genetically engineered plant. Calgene successfully petitioned for deregulation of its Flavr Savr tomato under this procedure.³

USDA has adopted a flexible regulatory strategy that avoids blanket determinations early in the history of an emerging new technology. For most crops, the agency requires premarket approval. For some species with lower risk, the agency is willing to play a monitoring role. Where the accumulated data justifies it, the agency will grant deregulated status.

Regulatory strategy of FDA

FDA's regulatory strategy is founded on a science-based approach and on the premise that genetic engineering is simply an extension of traditional breeding and of old biotechnology by application of new techniques. By regulating the products of genetic engineering and declining to regulate the process, FDA seeks to incorporate genetic engineering into its existing regulatory

framework, with minor modifications.¹⁴

FDA relies primarily on § 402(a)(1) of the Food, Drug, And Cosmetic Act (FDCA) to regulate food from genetically engineered plants. Any constituent of these foods that is newly introduced or expressed at higher levels following the manipulation is regarded as an added substance within the meaning of this section and thus regulated under the strict may render injurious to health standard. Food is adulterated if there is a reasonable possibility that its consumption will be injurious to health.¹⁵ This standard applies whether the alteration is intentional or inadvertent, and the producer bears legal responsibility for meeting it. FDA's policy is to guide the industry by formal guidelines and informal consultation, while reserving its formidable civil and criminal enforcement powers until breaches have occurred.¹⁶ The agency thus intends to play a consultative and policing rather than a licensing role.

Any substance intended as a food component, unless generally regarded as safe (GRAS), is subject to regulation under §§ 201(s) & 409 as a food additive. Food additives are banned unless exempted by regulation – i.e. they are subject to licensing by FDA. The agency's reluctance to play an extensive licensing role is evident in its published guidelines.

First, FDA adopts a narrow interpretation of the intended use test of § 201(s). The statutory language covers any substance the intended use of which results or may reasonably be expected to result, *directly or indirectly*, in its becoming a component *or otherwise affecting the characteristics of* any food... Despite this very broad language, FDA treats as potential food additives only the transferred genetic material and the resultant expression product.¹⁷ Second, FDA has adopted a broad view of GRAS. It states categorically that [i]ntroduced nucleic acids [i.e. foreign genetic material, in and of themselves, do not raise safety concerns. and are presumed GRAS.¹⁸ This is surprising in view of the concern that antibiotic resistance genes

ID # 103-8585-7

10

ingested in food may be transferred to gut bacteria and confer antibiotic resistance. The agency will presume as GRAS any introduced substance that is present in currently consumed foods at generally comparable or greater levels. However, any significant modification in structure, function or composition from substances found currently in food would raise a GRAS issue. Modifications are thus tested against substances found in the unmodified host food. FDA provides extensive guidance in recommending safety issues to be addressed, but once again leaves compliance with the food producer. There is no requirement for notification or prior approval; once again, the agency envisages a more limited consultative and policing role.

FDA has also shown reluctance to impose strict labeling requirements for genetically engineered foods. The agency asserts its broad power under § 403(i) combined with §§ 403(a) & 201(n) to require disclosure not only of a food's common or usual name, but also of any material difference from foods traditionally described by that name and of any material safety or usage issue. Yet FDA does not require disclosure that a food is genetically engineered, nor that proteins derived from other (donor) foods are present unless the donor food commonly produces allergic reactions. Even then, no disclosure is required if there is sufficient information showing that the (major) allergenic components of the donor food are known and are not present in the proteins introduced into the host food.⁹ The agency takes the view that genetic engineering techniques are merely extensions of traditional breeding methods and that the resulting foods do not differ from other foods in any meaningful or uniform way.

Evaluation of FDA's regulatory strategy

While FDA's general approach is scientifically sound, and its restrained approach undoubtedly within its statutory discretion, the agency appears to have erred on the side of under-

regulation, to the detriment of the industry it wishes to encourage.

The agency's decision to incorporate genetically engineered food into its existing regulatory structure seems wise. The very broad discretion and enforcement powers granted in the FDCA would permit virtually whatever regulation the agency wished to impose. By asserting a broad interpretation of the intended use test of § 201(s), together with a strict view of GRAS, FDA could impose a premarket approval regime for all genetically engineered foods. Similarly, its discretion on what disclosures are material for labeling is in practice unreviewable. By eschewing a request for new statutory powers, FDA avoided forcing on Congress a sensitive and emotive issue on which the general public has not yet had time to frame a considered opinion. Any Congressional action could scarcely have given FDA more effective powers; the only change likely to arise from new legislation would be an attempt to impose a stricter regulatory duty on the agency. If at all effective, the result would have been to lock in a rigid and inflexible regulatory regime.

Since FDA is operating within the realm of discretion, it should consider the following changes to its regulatory strategy:

- (1) A more subtly tailored licensing and notification regime.

USDA provides a regulatory model which is readily applicable to genetically engineered foods. While it is impractical and unnecessary to regulate each individual food item, the number of new plants is much more limited and could readily be regulated by a combined licensing and notification scheme. Genetically engineered modifications would in general require premarket approval. Where FDA was satisfied that a commonly used technique was safe (such as using the *k⁺sd* gene as an antibiotic resistance marker) it could be designated as approved and exempted from licensing. Even greater flexibility could be achieved by designating standards rather than individual genes (e.g. to ensure stable integration of the new genetic material in the host); this would approach

ID # 103-8585-7

12

the flexibility of the present guidelines. In all cases, however, the agency should insist on notification and should maintain a database of foods containing genetically engineered components. The agency should also consider imposing monitoring requirements for adverse reactions associated with the new products.

It is true, as FDA asserts, that genetic engineering is an extension of traditional breeding and other techniques, and that any change to a food crop may produce unintended effects. However, this does not justify turning a blind regulatory eye to possible adverse effects from one of the most powerful technologies known to mankind, and one that could rapidly and profoundly transform the human diet. Monitoring suspected allergic and other adverse reactions could give early warning of unforeseen problems and would allow FDA to forestall some future crisis that might jeopardize public acceptance of all genetically engineered foods.

Given the extensive consultation envisaged by FDA, and conducted with the pioneering products currently approaching market, this new regime would not greatly increase the industry's regulatory burden. Indeed, recent developments suggest that the industry might prefer tighter regulation to help it overcome public hesitancy about the new technology. The perception, of unbridled deregulation is deeply damaging to this emerging sector, as the FDA Commissioner frankly admitted? Moreover, Calgene has requested that FDA regulate the *ka⁻* gene and its enzyme product as food additives in order to help correct misunderstanding by the public as to the scope and rigor of FDA's review of new [genetically engineered] food products[,...] underscore the adequacy of the FDA policy and provide confidence to the public. ... 21 The potential for adverse public reaction was underscored when prominent restaurateurs announced a boycott of genetically engineered foods, and when Campbell Soup Co. canceled plans to use the Flav'r Savr tomato, apparently in response to public pressure.

ID # 103-8585-7

13

(2) Stricter labeling requirements

FDA has not persuasively justified its refusal to treat the fact that a food is genetically engineered, and the species of origin of the genetically introduced protein as material facts requiring disclosure. Consumers with religious, moral or aesthetic scruples are entitled to decide for themselves whether the essential nature of a food has been altered, whatever FDA concludes. Consumers who are allergic to some foods are entitled to fair warning that an apparently familiar food may contain new ingredients, so that they may take appropriate precautions. Fortunately, FDA appears to be rethinking its position in the light of comments responding to its 1992 Statement of Policy.[~]

Calgene's marketing plans illustrate the feasibility of labeling genetically engineered fruits and vegetables, since the company intends to mark each tomato with a circular label. The proposed wording, however, illustrates the need for regulation. The label will identify the product as Macgregor's Tomatoes. Grown From Flav'r Savr Seeds. Point of sale information will disclose use of the latest developments in genetic engineering, tomato plant breeding, and farming as well as insertion of a gene which makes a naturally occurring protein [that] makes Flav'r Savr seeds resistant to kanamycin contained in our test medium.²³ Taken as whole, this seems fair. Without the point of sale information, however, the label's folksy name would be misleading. Without regulatory deterrence, unscrupulous producers (or retailers) might be tempted to omit disclosing the use of genetic engineering, especially if such products encounter consumer resistance.

(3) Imposing Current Good Manufacturing Practice requirements

FDA has asserted the power under § 70 1(a) to impose CGMP requirements for food manufacturing, processing and storage and has used its authority to impose recordkeeping duties.[~] This section provides an alternative source of authority for requiring producers and retailers to keep

track of genetically engineered foods, whether sold as raw produce or incorporated into processed foods. This authority could also be used to impose technical standards for insertion of genetic material (e.g. stable insertion of well-characterized constructs) even if FDA wishes to avoid treating these components as additives.

~Qn~Qn

In framing a regulatory response to new technologies that affect the food supply, FDA must deal not only with legal and scientific issues, but also with popular perceptions. The public holds the agency in high regard and trusts it to ensure the safety and accurate identification of foods. This mandate the agency must not only discharge, but also be seen to discharge. FDA's present approach to genetically engineered plants is scientifically and legally defensible, but takes too little account of public perceptions. In seeking to encourage the food biotechnology industry, FDA is harming it through under-regulation.

1. S~ David A. Kessler et al., The Safety of Foods Developed by Biotechnology, 256 Science 1747, 1747 (1992).
2. S~ Food and Drug Administration, Statement of Policy: Foods Derived From New Plant ~ 57 Fed. Reg. 22,984, 22,985-86 (1992).
3. Kessler et al., 256 Science at 1747. Examples of the types of genetically engineered crops under development are tabulated at 1748.
4. ~ American Medical Association (Council on Scientific Affairs), Biotechnology and the American Agricultural Industry, 265 J. Am. Med. Ass'n 1429 (1991) which briefly reviews several of these applications.
5. S~ 58 Fed. Reg. 17,044 (1993), to be codified at 7 C.F.R. § 340, promulgating the regulatory regime for genetically engineered plants of Animal and Plant Health Inspection Service (APHIS), USDA.
6. ~ USDA, Animal and Plant Health Inspection Service, Interpretive Ruling on Calgene. Inc. r Petition for Determination of Regulatory Status of FLAVR SAVR Tomato, 57 Fed. Reg.

ID # 103-8585-7

15

47,608, 47,613-14 (1992).

7. ~ Food Chemical News, Sept. 6, 1993, at 18-19; 1d.~, Sept. 20, 1993 at 15-16.

8. ~ Food Chemical News, Feb. 22, 1993 at 18-19.

9. ~ Food and Drug Administration, Food Labeling: Foods Derived From New Plant Varieties (Request for data and information), 58 Fed. Reg. 25,837, 25,839 (1993).

10. S~ Dick Russell, Miia~k.f..Myth~, The Amicus J., Spring 1993, at 20.

11. ~ Jonathan W. King, Breeding Uniformity, The Amicus J., Spring 1993, at 25.

12. ~ 58 Fed. Reg. 17,044 (1993).

13. ~ 57 Fed. Reg. 47,608, 47,613-14 (1992).

14. ~ 57 Fed. Reg. 22,984 (1992).

15. ~ United States v. Lexington Mill & Elevator Co., 232 U.S. 399 (1914).

16. Under § 406, FDA has power to establish tolerances for poisonous or deleterious substance[s that are] required in the production [of a food or that] cannot be avoided by good manufacturing process ... The agency has avoided using these powers on this issue.

17. 57 Fed. Reg. at 22,990.

18. 57 Fed. Reg. at 22,990, 23,004.

19. ~ 57 Fed. reg. at 22,991.

20. ~ Food Chemical News, Apr. 26, 1993 at 13, reporting Dr. David Kessler's remarks on the reduction of public confidence in FDA's food biotechnology policy that arose through association with the Council on Competitiveness. Everyone would have been better served if

we had just let it be published in 'Science

21. Letter from Donald L. Emlay, Director, Regulatory Affairs, Calgene, Inc. to Dr. Alan M.

Rulis, Director, Office of Premarket Approval, FDA (Jan. 4, 1993). ~ Food Chemical News, Jan 11, 1993 at 31.

22. ~ 58 Fed. Reg. 25,837 (1993), inviting further comments on this issue.

23. ~ Food Labeling News, Oct. 28, 1993.

24. Even this labeling raises an issue: the kanamycin resistance gene does indeed occur naturally, but only in E. coli, a pathogenic gut bacterium.

ID # 103-8585-7

16

25. ~ 51 Fed. Reg. 22,458 (June 19, 1986).
ID # 103-8585-7 17